SUPPORT FOR THE AMENDMENTS

Claims 2 and 44-49 have been amended.

The amendment of Claim 2 is supported by page 11, line 25 to page 12, line 6 of the specification. The amendment of Claims 44-49 is supported by original Claims 1 and 2, the corresponding previously pending claims, and page 11, line 25 to page 12, line 6 of the specification.

No new matter has been entered by the present amendment.

REMARKS

Claims 1-49 are pending in the present application.

The rejections of: (a) Claims 1-11, 19-27, and 42 under 35 U.S.C. §112, first paragraph (enablement), and (b) Claims 1-11, 19-27, and 42 under 35 U.S.C. §112, first paragraph (written description), are believed to be obviated by amendment.

In the outstanding Office Action, the Examiner alleges that "Nucleotide sequences encoding proteins with 95% identity to the 364 amino acid long SEQ ID NO: 2 would encode proteins with 18[1] amino acid substitutions relative to SEQ ID NO: 2". The Examiner's focus in this context is that there are 18 possible "unspecified amino acid changes within the amino acid sequence of SEQ ID NO: 2". The Examiner alleges that absent guidance as to what amino acid residues could be changed to preserve activity the claims cannot satisfy the written description or enablement requirements.

This allegation by the Examiner is without merit. This is precisely the question taken up by Example 14 of the Synopsis of Application of Written Description Guidelines which analyzes a situation where a claim covers a protein that is at least 95% identical to a disclosed sequence and has a specific function. In these guidelines, the Office concluded that such a claim is adequately described within the meaning of 35 U.S.C. § 112, first paragraph. Indeed, as argued in the response filed on August 20, 2007, Example 14 of the Synopsis of Application of Written Description Guidelines is representative of the claimed invention and provides:

> There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have

[1] In the original text, the Examiner inadvertently inserts "18%" where "18" should have been used. Clearly, when the homologous protein has 95% identity to a 364 amino acid long protein, the maximum number of mutations permitted is 18.

> substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed ***is representative*** of the genus because all members have at least *95%* structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least *95%* identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus.
>
> **Conclusion:** The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.

The specification clearly provides sufficient description of the actual reduction to practice of a single disclosed species (i.e., SEQ ID NO: 2). Further, the specification describes how the skilled artisan can test for the recited activity to readily determine whether the variants are capable of the specified catalytic activity. Therefore, Claim 1 is described and enabled. The Examiner comments on page 7, third paragraph, further emphasize the fact that the skilled artisan would readily eliminate non-operative species as these fail to meet the required activity limitation.

Further with respect to Example 14 of the Synopsis of Application of Written Description Guidelines, the Examiner alleges that the:

> "instant claims directed to 95% sequence identity to SEQ ID NOs: 1 or 2 is not analogous to the claim in Example 14 of USPTO guidelines on written description. The claim of Example 14 of guidelines recites 95% sequence identity to SEQ ID NO: 3 which encompasses a significantly small genus of sequences, as compared to instant claims 1, and 45-46 which recite 95% sequence identity to SEQ ID NO: 2 or claims 2 and 47-48 which recite 95% sequence identity to SEQ ID NO: 1." (page 9, lines 7-12 of the Office Action mailed November 16, 2007)

With respect to the allegations as they related to Claim 2, Applicants address the same below in relation to amended Claims 2 and 47-48. However, this allegation is without merit as it applies to Claims 1 and 45-46.

The Examiner is referred to Example 14 of the Synopsis of Application of Written Description Guidelines. At no point does the Office specify either the size of the "protein having SEQ ID NO: 3" or the size of the genus of sequence variants in this Example.

Accordingly, the Examiner's allegation that "The claim of Example 14 of guidelines recites 95% sequence identity to SEQ ID NO: 3 which encompasses a significantly small genus of sequences, as compared to instant claims 1, and 45-46 which recite 95% sequence identity to SEQ ID NO: 2" is inaccurate. It must be emphasized that Example 14 does not limit and/or specify the size of the protein of SEQ ID NO: 3 recited therein. Therefore, the size of the genus defined in Claim 1 is easily the *same* size as or even *smaller* in size than that of Example 14 of the Synopsis of Application of Written Description Guidelines. Accordingly, Applicants submit that Claim 1 and the claims dependent therefrom are fully described and enabled by the specification.

Claim 2 has been amended to define (e) and (f) as "a DNA encoding a protein consisting of an amino acid sequence at least 95% homologous to the amino acid sequence of SEQ ID NO: 2 and having [recited] activity." Applicants submit that such a claim is fully described and enabled for the reasons given above and further explained below. Specifically, Applicants refer the Examiner to at least the following three authorities, which clearly establish the sufficiency of the present specification vis-à-vis the written description requirement of 35 U.S.C. §112, first paragraph:

1) Example 11 of the Synopsis of Application of Written Description Guidelines;
2) MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 6, 2007); and
3) *In Re Wallach* 378 F3d 1330, 71 USPQ2d 1939 (Fed. Cir. 2004), copy **submitted herewith**.

First, in Example 11 of the Synopsis of Application of Written Description Guidelines, the following facts are presented:

> **Specification:** The specification discloses a DNA, SEQ ID NO: 1, said to encode a cell surface receptor for adenovirus. The cell surface receptor is designated protein X and its sequence is given as SEQ ID NO:2. The specification states that the invention includes alleles of the

> DNA that include single nucleotide polymorphisms (SNPs). No allelic sequence information is disclosed, but the specification states that allelic variants of SEQ ID NO: 1 can be obtained, e.g., by hybridizing SEQ ID NO: 1 to a DNA library made from the species of organism that yielded SEQ ID NO: 1.

Against this background, the following Claim 1 is presented:

1. An isolated DNA that encodes protein X (SEQ ID NO: 2).

And, the Guidelines then provide the following analysis finding that written description is present:

> **Analysis:**
> **Claim 1:**
> Claim 1 is drawn to the genus of DNAs that encode amino acid sequence SEQ ID NO:2, i.e., all sequences degenerately related by a genetic code table to SEQ ID NO:1. Although only one specie within the genus is disclosed, SEQ ID NO:1, a person of skill in the art could readily envision all the DNAs degenerate to SEQ ID NO:1 by using a genetic code table. One of skill in the art would conclude that applicant was in possession of the genus based on the specification and the general knowledge in the art concerning a genetic coding table.

True, in Example 11 above, the facts state that the specification provides "only one species within the genus". However, in this example, emphasis is placed on the general knowledge in the art and the ready application of the genetic coding table to arrive at all possible polynucleotides that encode the claimed amino acid sequence. This general ability is directly applicable to the claimed invention.

MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 6, 2007) recognizes this general ability existing in the art and removes even the need to disclose any possible polynucleotides that encode the claimed amino acid sequence. Specifically, MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 6, 2007) recites:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, ***it would be unnecessary to provide an explicit disclosure of***

> ***nucleic acid sequences that encoded the amino acid sequence***. Since the genetic code is widely known, ***a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence***, but not necessarily any particular species. Cf. *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). (*emphasis added*)

From the foregoing, it is clear that the specification need not provide even a single example of a polynucleotide that encodes the claimed amino acid sequence in order to meet the written description guidelines. All that is required is the full amino acid sequence, which was provided in the Sequence Listing as filed in the present application and in accordance with the Example 14 of the Synopsis of Application of Written Description Guidelines descriptive support is also present for amino acid sequences having 95% homology to SEQ ID NO: 2.

Moreover, the Courts have already opined in *In re Wallach* that applications similarly situated to the present application meet the written description requirement. Specifically, the Court in *In re Wallach* stated:

> As a preliminary matter, ***we agree with Appellants that the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art at the time the '129 application was filed may have therefore been in possession of the entire genus of DNA sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious***. Cf. In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995). Thus, for example, the RNA molecules required to encode the described amino acid sequence must necessarily have the following sequence: ACN-CCN-UAY-GCN-CCN-GAR-CCN-GGN-(UCN or AGY)-ACN, where N is A, G, C, or U; Y is U or C; and R is G or A. See James D. Watson et al., Molecular Biology of the Gene 356-57 (3d ed. 1977), cited in '129 application. A claim to the genus of DNA molecules complementary to the RNA having the sequences encompassed by that formula, even if defined only in terms of the protein sequence that the DNA molecules encode, while containing a large number of species, is definite in scope and provides

the public notice required of patent applicants. Indeed, the PTO's Manual of Patent Examining Procedure ("MPEP") states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.
>
> MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 2 2001).

Moreover, we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that ***it is***, as explained above, ***a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it.*** (*emphasis added*)

Based on the foregoing, Applicants submit that the explicit disclosure of SEQ ID NO: 2 in the original Sequence Listing, the disclosure of variants that are at least 95% homologous to SEQ ID NO: 2, and elsewhere in the specification provides clear written description support for the full scope of polynucleotides encoding an amino acid sequence at least 95% homologous to the amino acid sequence of SEQ ID NO: 2 and having [recited] activity.

Further, with respect to enablement, Applicants remind the Examiner that MPEP § 2164.01 states:

> "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."

Applicants respectfully submit that the skilled artisan can introduce mutations into SEQ ID NO: 2 by conventional that are generally and widely known and available. Further, with the specification in hand the artisan could readily practice the claimed invention without undue experimentation, especially when the disclosure is augmented with the information known in the art.

Further, MPEP §2164.04 states:

> "A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

The specification is replete with references to describe appropriate methods of isolating, cloning, transforming bacteria, and culturing bacteria harboring the claimed sequences including SEQ ID NO: 2. Moreover, Applicants provide detailed examples showing how to clone the claimed sequences and how to monitor for this activity. Applicants submit that, in view of the guidance proffered by the present specification, determining the identity of sequences that fall within the scope of the claimed invention would require nothing more than routine skill in the art.

Withdrawal of these grounds of rejection is requested.

The objection to Claims 44-49 is obviated by amendment.

Applicants have amended the claims consistent with the Examiner suggestions. Accordingly, this ground of objection is believed to be moot.

Withdrawal of this ground of objection is requested.

Finally, the objection to the drawings is obviated in part by amendment and traversed in part.

In paragraph 3 of the Office Action, the Examiner alleges that Figure 17 fails to comply with 37 CFR 1.84(g) "it is maintained that Figure 17 is framed because all the existing labels (see numbers 1-5) are within the box". Applicants disagree with this allegation by the Examiner, but at least wish to thank the Examiner for further clarifying the basis for his allegation. Applicants maintain that it is clear based on the illustration that Figure 17 shows the results of genomic Southern hybridization described in Example 8. The solid line in Figure 17 is not a "frame" as the Examiner alleges, but rather is an illustration of the outer boundary of the membrane to which the content of the electrophoretic gel was transferred. Thus, the solid line in Figure 17 is not a "frame", but rather a part of the illustration. Nonetheless, since Applicants do not wish to prolong prosecution over a relatively minor point that has no basis on the interpretation of any claims and/or substance of this application, Applicants submit herewith a replacement Figure 17 wherein the outer boundary of the membrane to which the content of the electrophoretic gel was transferred has been deleted. Therefore, this criticism is believed to be moot.

The Examiner also objects to Figure 17 alleging that this figure lacks molecular size markers and that it is "absolutely important to know the molecular size of hybridizing band so that one skilled in the art can distinguish what is being hybridized within the restriction enzyme digested plant genome". Applicants again disagree with this objection and the Examiner's allegations in an attempt to support this objection. Specifically, Applicants submit that there is no requirement for an electrophoretic gel to contain molecular size markers. Further, Applicants submit that the specification and Figure 17 sufficiently describe the results set forth in this figure. As explained in Example 8 (see page 45, lines 12-15), the

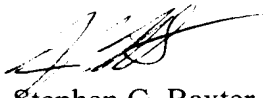
assay illustrated in Figure 17 was performed only to confirm the number of copies of the introduced gene in the genomic DNA. Moreover, the Examiner should note that this figure is not required to support and/or enable the claimed invention. This figure is only provided to further illustrate a result that is clearly spelled out in the specification. The result in Figure 17 is clear and size determination is not required. As such, no further amendment is necessary to account for this alleged deficiency.

In view of the foregoing, Applicants request withdrawal of this ground of objection.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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United States Court of Appeals for the Federal Circuit

03-1327
(Serial No. 08/485,129)

IN RE DAVID WALLACH, HARTMUT ENGELMANN,
DAN ADERKA, DANIELA NOVICK, and MENACHEM RUBINSTEIN

Roger L. Browdy, Browdy and Neimark, P.L.L.C., of Washington, DC, argued for appellants.

Mary L. Kelly, Associate Solicitor, Office of the Solicitor, United States Patent and Trademark Office, of Arlington, Virginia, argued for the Director of the U.S. Patent and Trademark Office. With her on the brief were John M. Whealan, Solicitor; and Raymond T. Chen, Associate Solicitor. Of counsel were Stephen Walsh and William LaMarca, Associate Solicitors.

Appealed from: United States Patent and Trademark Office
Board of Patent Appeals and Interferences

United States Court of Appeals for the Federal Circuit

03-1327
(Serial No. 08/485,129)

In re DAVID WALLACH, HARTMUT ENGELMANN,
DAN ADERKA, DANIELA NOVICK and MENACHEM RUBINSTEIN

DECIDED: August 11, 2004

Before MAYER, Chief Judge, LOURIE and GAJARSA, Circuit Judges.

LOURIE, Circuit Judge.

David Wallach, Hartmut Engelmann, Dan Aderka, Daniela Novick, and Menachem Rubinstein (collectively, "Appellants") appeal from the decision of the United States Patent and Trademark Office ("PTO") Board of Patent Appeals and Interferences affirming the rejection of claims 11-13, 35-38, 43, 44, 46-49, 51-54, 56-61, 63, and 64 of United States patent application 08/485,129 under the written description requirement of 35 U.S.C. § 112. In re Wallach, Appeal No. 2002-1363 (Bd. Pat. Apps. & Interfs. Dec. 26, 2002). We affirm.

BACKGROUND

In the 1980s, Appellants apparently discovered two specific proteins isolated from human urine that, among other things, selectively inhibit the cytotoxic effect of tumor necrosis factor ("TNF"). They named the compounds TNF binding proteins I & II ("TBP-I" and "TBP-II"). After obtaining a partial amino acid sequence of the N-terminal portion of TBP-II and determining that the complete protein has a molecular weight of about 30 kilodaltons ("kDa") when measured by sodium dodecyl sulfate polyacrylamide gel electrophoresis ("SDS-PAGE") under reducing conditions, Appellants filed a patent

application including, inter alia, claims directed to proteins having that molecular weight and partial sequence (i.e., threonine-proline-tyrosine-alanine-proline-glutamic acid-proline-glycine-serine-threonine, or "Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr") and having the ability to inhibit the cytotoxic effect of TNF. Appellants' application also included claims to isolated DNA molecules that encode the claimed proteins. The PTO issued a restriction requirement and Appellants filed divisional applications. The claims directed to the proteins having the stated partial sequence are currently involved in an interference proceeding and are not at issue here. The claims at issue, those directed to the DNA, were rejected under § 112 "as based on a specification which does not provide an adequate written description of the claimed invention." Wallach, slip op. at 2. After several unsuccessful attempts to traverse that rejection, Appellants appealed to the Board.

Citing this court's decisions in Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed. Cir. 1991), Fiers v. Revel, 984 F.2d 1164 (Fed. Cir. 1993), and Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559 (Fed. Cir. 1997), the Board affirmed the examiner's rejection. In particular, the Board held that "(1) applicants do not describe the genetic material sought to be patented in claim 11 with sufficient specificity in their specification; and (2) the examiner did not err in finding that claim 11 is based on a specification which does not provide adequate, written descriptive support for the claimed subject matter." Wallach, slip op. at 8-9.[1]

Appellants now appeal. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(4)(A).

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[1] The Board treated all of the appealed claims as standing or falling together with claim 11, pursuant to 37 C.F.R. § 1.192(c)(7), and decided the appeal on the basis of that claim alone. Wallach, slip op. at 5. Appellants do not challenge the Board on that point, and we likewise decide this appeal only on the basis of that claim.

DISCUSSION

Claim 11 of the '129 application reads as follows:

> 11. An isolated DNA molecule comprising a contiguous nucleotide sequence coding for a protein consisting of naturally occurring human Tumor Necrosis Factor (TNF) Binding Protein II, herein designated TBP-II, said TBP-II including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr in the portion of the protein sequenced by N-terminal sequence analysis, said protein having the ability to inhibit the cytotoxic effect of TNF, wherein said naturally occurring TBP-II protein is the same as that protein having the ability to inhibit the cytotoxic effect of TNF which, after being purified by subjecting a crude protein recovered from a dialyzed concentrate of human urine to affinity chromatography on a column of immobilized TNF, elutes from a reversed-phase high pressure liquid chromatography column as a single peak in a fraction corresponding to about 31% acetonitrile and shows a molecular weight of about 30 kDa when measured by SDS-PAGE under reducing conditions.

On appeal, Appellants argue that the PTO has effectively conceded that the TBP-II protein, which the claimed isolated DNA encodes, is sufficiently described in the specification to comply with § 112, because the claims of United States patent application 07/930,443, of which the '129 application is a division (which, by definition, has the same specification), have been allowed but for their involvement in an interference proceeding. According to Appellants, those claims do not differ in substance from the present claims except insofar as they are directed to a partial protein sequence, rather than to the DNA sequences encoding the protein. Appellants contend that that is not a meaningful distinction, because the genetic code is based on an unequivocal correspondence between amino acids and encoding DNA codons, and determination of the amino acid sequence of a protein automatically puts one in possession of all DNA sequences encoding that protein. Appellants also argue that the complete amino acid sequence of a protein is an inherent property of an isolated protein that has been fully characterized by partial amino acid sequence and other characteristics, and that the complete amino acid

sequence of a protein therefore puts one in possession of all DNA sequences encoding it. Therefore, according to Appellants, the specification establishes that the present inventors were in fact in possession of the entire claimed genus of DNA sequences at the time the application was filed.

Appellants also argue that this case is distinguishable from past written description cases such as Amgen v. Chugai and Fiers, because Appellants have provided an actual amino acid sequence that is encoded by the claimed DNA, not simply the name of the protein and a statement that the DNA can be obtained by reverse transcription. Appellants contend that this case is also distinguishable from Lilly because the inventors here are not attempting to claim DNA molecules encoding a plurality of unknown proteins from various species having no common features, but only those encoding the single protein sequence that is actually set forth in the specification. Finally, Appellants argue that, because there is a known correlation between the function (i.e., encoding a specified amino acid sequence) and structure, this is the quintessential example of the sort of functional description permitted by § 112 in view of our decision in Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316 (Fed. Cir. 2002). Appellants argue that our recent decision in Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313 (Fed. Cir. 2003), which issued after the Board's opinion in the present case, reaffirmed that § 112 only requires a court to determine whether a specification conveys to one of ordinary skill in the art as of the filing date that the inventors invented the claimed subject matter.

The PTO responds by arguing that Appellants' specification includes neither any actual DNA sequence within the scope of the claims nor the complete amino acid sequence of the TBP-II protein, but only the sequence of ten out of the 185-192 amino

acids that make up the protein. Furthermore, the PTO argues, the only disclosed function of the claimed DNA molecules is to encode the TBP-II protein, and no information is provided from which the claimed DNA molecules can be distinguished from other DNA molecules. According to the PTO, the identity of the nucleic acid encoding a protein is not an inherent property of the protein. If Appellants' reasoning were accepted, the PTO asserts, the result would be that the disclosure of an isolated protein would be prior art under § 102 with respect to claims directed to any nucleic acid encoding the protein. Finally, the PTO contends, substantial evidence supports the Board's factual finding that Appellants' specification does not adequately describe the claimed genus of DNA molecules.

As a preliminary matter, we agree with Appellants that the state of the art has developed such that the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it, and that one of ordinary skill in the art at the time the '129 application was filed may have therefore been in possession of the entire genus of DNA sequences that can encode the disclosed partial protein sequence, even if individual species within that genus might not have been described or rendered obvious. Cf. In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995). Thus, for example, the RNA molecules required to encode the described amino acid sequence must necessarily have the following sequence: ACN-CCN-UAY-GCN-CCN-GAR-CCN-GGN-(UCN or AGY)-ACN, where N is A, G, C, or U; Y is U or C; and R is G or A. See James D. Watson et al., Molecular Biology of the Gene 356-57 (3d ed. 1977), cited in '129 application. A claim to the genus of DNA molecules complementary to the RNA having the sequences encompassed by that formula, even if defined only in terms of the protein sequence that

the DNA molecules encode, while containing a large number of species, is definite in scope and provides the public notice required of patent applicants. Indeed, the PTO's Manual of Patent Examining Procedure ("MPEP") states:

> Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, but not necessarily any particular species.

MPEP § 2163.II.A.3.a.ii. (8th ed., rev. 2 2001).

Moreover, we see no reason to require a patent applicant to list every possible permutation of the nucleic acid sequences that can encode a particular protein for which the amino acid sequence is disclosed, given the fact that it is, as explained above, a routine matter to convert back and forth between an amino acid sequence and the sequences of the nucleic acid molecules that can encode it.

Nonetheless, Appellants did not claim the nucleic acid molecules that encode the simple protein sequence that they disclosed. Rather, they claimed the nucleic acids encoding a protein for which they provided only a partial sequence. Appellants concede that it is now known that urinary TBP-II has a sequence of 185-192 amino acids. Without the approximately 95% of the amino acid sequence that Appellants did not disclose, we cannot say that the DNA molecules claimed in the '129 application have been described. As the MPEP explains, "disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention." MPEP § 2163.II.A.3.a.i. The Board's decision was thus consistent with its guidance in the

MPEP. Here, Appellants disclosed a partial structure and possibly sufficient additional characterization of the TBP-II protein to satisfy the PTO that they were in possession of the claimed subject matter in their '443 application, but that additional characterization contributes little, if anything, to the description of the DNA molecules claimed in the '129 application.

Appellants argue that "[a]s appellants have demonstrated possession of the TBP-II protein, appellants were also necessarily in possession of its inherent amino acid sequence, as well as all of the DNA sequences encoding that amino acid sequence." We disagree. Whether Appellants were in possession of the protein says nothing about whether they were in possession of the protein's amino acid sequence. Although Appellants correctly point out that a protein's amino acid sequence is an inherent property of the protein, the fact that Appellants may have isolated and thus physically possessed TBP-II does not amount to knowledge of that protein's sequence or possession of any of its other descriptive properties. Appellants have not provided any evidence that the full amino acid sequence of a protein can be deduced from a partial sequence and the limited additional physical characteristics that they have identified. Without that full sequence, we cannot agree with Appellants that they were possession of the claimed nucleic acid sequences. In Amgen v. Chugai, we explained that:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, . . . because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

927 F.2d at 1206. Until Appellants obtained the complete amino acid sequence of TBP-II, they had no more than a wish to know the identity of the DNA encoding it.

As Appellants point out, we have recognized that the written description requirement can in some cases be satisfied by functional description. See, e.g., Enzo, 296 F.3d at 1324 ("It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement."). Nonetheless, such functional description can be sufficient only if there is also a structure-function relationship known to those of ordinary skill in the art. As we explained above, such a well-known relationship exists between a nucleic acid molecule's structure and its function in encoding a particular amino acid sequence: Given the amino acid sequence, one can determine the chemical structure of all nucleic acid molecules that can serve the function of encoding that sequence. Without that sequence, however, or with only a partial sequence, those structures cannot be determined and the written description requirement is consequently not met. As we explained in Enzo, the Guidelines for Examination of Patent Applications under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099 (Jan. 5, 2001) ("Guidelines"), state that

> the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, 66 Fed. Reg. at 1106 (emphasis added).

Enzo, 296 F.3d at 1324-25 (emphasis added). Appellants have provided no evidence that there is any known or disclosed correlation between the combination of a partial structure of a protein, the protein's biological activity, and the protein's molecular weight, on the one hand, and the structure of the DNA encoding the protein on the other.

CONCLUSION

The Board correctly affirmed the examiner's determination that the specification of the '129 application does not provide an adequate written description of the pending claims. Accordingly, the Board's decision is

AFFIRMED.